acceptable salt thereof, wherein the moisture content of the poly(allylamine) is from about 5% to about 9% by weight, wherein the hardness of the tablet is at least about 150 N and wherein the friability of the tablet is no more than 0.8%.

a2 23. (New) A tablet comprising a core and a coating therefor, wherein the core comprises 98% by weight sevelamer hydrochloride with a moisture content of 6% by weight, 1% by weight colloidal silicon dioxide and 1% by weight stearic acid, and wherein the coating is a mixture comprising 38.5% w/w low viscosity hydroxypropylmethylcellulose, 38.5% high viscosity hydroxypropylmethylcellulose and 23% w/w diacetylated monoglyceride.

REMARKS

Information Disclosure Statement

In the text of the Office Action, the Examiner acknowledges Information Disclosure Statements filed in August and October 2001. However, the Examiner has only initialed and returned Information Disclosure Statements filed in October 2000 and August 2001. Applicants request that an initialed copy of the Second Information Disclosure Statement, filed October 2, 2001, be returned in the next Office Action.

Priority Claim Under 35 U.S.C. 119(e)

Applicants have claimed priority to U.S. Provisional Application No. 60/160,258 filed October 19, 1999 and U.S. Provisional Application No. 60/174,227, filed January 3, 2000. The priority claim was not acknowledged in the present Office Action. The Examiner is respectfully requested to acknowledge the priority claim in the next Office Action.

Claim Amendment

Claim 2 been rewritten in independent form, incorporating all the limitations of cancelled Claim 1. Claims 5, 6, and 13, originally dependent on Claim 1, have been amended to depend on Claim 2.

Claims 2, 7, and 12 have been amended to recite "a tablet comprising a core and coating therefor," rather than a tablet core. Support for the amendment can be found at page 5, lines 6-8 of the specification. Dependent claims 3-6, 8-11, and 13-18 have been amended accordingly.

Claim 4 has been amended to recite that alkyl groups can be substituted alkyl groups such as a trialkylammonioalkyl group. Support for amended Claim 4 can be found at page 4, lines 9-10 of the specification.

Claim 19 have been amended to recite that a compressed tablet comprises a pharmaceutically active agent and polyallylamine. Support for amended Claim 19 can be found at page 6, lines 17-23.

Support for new Claim 21 can be found at page 4, lines 15-18 and page 10, lines 18-21.

Support for new Claim 22 can be found in Examples 1 and 2 (pages 8-10).

Rejection of Claim 4 Under 35 U.S.C. §112, Second Paragraph

The Examiner states that Claim 4 is indefinite, because it is unclear how the alkyl substituents are further limited. Applicants have amended Claim 4 to recite that the alkyl substituents are trialkylammonioalkyl groups. Reconsideration and withdrawal of the rejection are requested.

Rejections of Claims 1-8, 12, and 19-21 Under 35 U.S.C. §102(b)

A. Summary of the Rejection

The Examiner states that Claims 1-8, 12, and 19-21 are anticipated by U.S. Pat. No. 5,496,545 (hereinafter "the '545 Patent"). The Examiner states that the '545 Patent relates to phosphate-binding polymers, such as polyallylamine, to be orally administered for the treatment of hyperphosphatemia. The Examiner further states that in a pharmaceutical composition, these polymers can be admixed with a carrier or enclosed within a carrier to form a tablet or capsule. The Examiner states that suitable carriers include cellulose and methyl cellulose.

B. Summary of the '545 Patent

The '545 Patent discloses polymers capable of removing phosphate from the gastrointestinal tract. The '545 Patent additionally discloses a method of removing phosphate

from the gastrointestinal tract, which involves administering a pharmaceutical composition of a phosphate-binding polymer. The '545 Patent teaches that pharmaceutical compositions can be in the form of capsules, tablets, pills, powders, and others. However, the '545 Patent does not teach the proportion of polymer in a tablet or capsule. Also, the '545 Patent does not teach the desirability of minimizing the amount of excipients in a pharmaceutical composition.

C. Claims 1-8 and 12 Are Not Anticipated by the '545 Patent

In order for the present claims to be anticipated by the '545 Patent, each and every element of the present claims must be disclosed in the '545 Patent. The instant claims require the tablet core to comprise at least 95% by weight of an aliphatic amine polymer. However, the '545 does not disclose the proportion of phosphate-binding polymer in a tablet. Instead, the '545 Patent states:

> In making the compositions of the present invention, the polymeric phosphate binder may be present alone, may be admixed with a carrier, diluted by a carrier, or enclosed within a carrier which may be in the form of a capsule, sachet, paper, or other container. When the carrier serves as a diluent, it may be a solid, semi-solid or liquid material which acts as avehicle, excipient or medium for the polymer. Thus, the compositions can be in the form of tablets, pills, powders, lozengers, sachets, cachets, elixirs, suspensions, syrups, aerosols (as a solid or in a liquid medium), soft or hard gelatin capsules, sterile packaged powders, and the like. (Column 17, lines 30-41)

The present application teaches at Page 1, line 19 to Page 2, line 8 teaches that it is generally not possible to render a polymer into a tablet without a significant addition of other materials. Therefore, it is clear that a polymer must be mixed with some amount of carrier in order to form a tablet or tablet core, but the amount of carrier is not disclosed in the '545 Patent. Thus, the limitation that a tablet core comprises at least 95% by weight of an aliphatic amine polymer or polyallylamine distinguishes Claims 1-8 and 12 from the '545 Patent.

D. Claims 19-21 Are Not Anticipated by the '545 Patent

The limitation that the tablet comprise a pharmaceutically active agent and polyallylamine distinguishes Claims 19-21 from the '545 Patent. There is no teaching in the '545 Patent of a tablet comprising both ingredients.

Therefore, Applicants have demonstrated that the '545 Patent does not disclose every element of Claims 1-8, 12, and 19-21, because the '545 Patent does not disclose the amount or proportion of an aliphatic amine polymer (e.g., polyallylamine) in a tablet or tablet core and does not disclose the combination of an aliphatic amine polymer and a pharmaceutically active agent. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-21 Under 35 U.S.C. §103(a) Over the '545 Patent in view of Renagel (Physicians' Desk Reference)

A. Summary of the Rejection

The Examiner states the Claims 1-21 are rejected as being obvious over the '545 Patent in view of disclosures relating to Renagel (i.e., in the specification and in the Physicians' Desk Reference [hereinafter "PDR"]). The Examiner further states the '545 Patent teaches Renagel has been shown to be effective at removing phosphate from human patients suffering from renal failure. The Examiner states the PDR shows that Renagel is film-coated, and the tableted forms contain hydroxypropyl methylcellulose. The Examiner reasons that one skilled in the art would be motivated to use the tableted forms of Renagel for administering the pharmaceutical compositions of the '545 Patent.

B. Response for Claims 1-18

The instant application claims priority to U.S. Provisional Application No. 60/160,258 filed October 19, 1999 and U.S. Provisional Application No. 60/174,227, filed January 3, 2000. The cited reference from the PDR was issued in July 2000. Therefore, the PDR is not available as prior art in examining the instant application.

Renagel was first available (see "Exhibit A", taken from the URL www.genzymetherapeutics.com/renagel/welcomeindex.htm, second paragraph) in November

1998, albeit in a capsule formulation. The present claims are directed to a tablet. A Renagel capsule and a tablet of the present invention are significantly different. Stedman's Medical Dictionary, 27th Ed., defines a capsule as:

> a solid dosage form in which a drug is enclosed in either a hard or soft soluble **container or "shell"** of a suitable form of gelatin (emphasis added, p.280, "Exhibit B"),

whereas a tablet is:

> a solid dosage form containing medicinal substances with or without suitable diluents; it may vary in shape, size, and weight, and may be classed according to the method of manufacture, [such] as [a] compressed tablet (p. 1781, "Exhibit C").

Therefore, it can be concluded that a tablet and a capsule are not equivalent, as the gelatin of a capsule acts as a container for a capsule. No such container is required or desired in a tablet.

The present application teaches at page 1, line 22 to page 2, line 2 that not all therapeutics, particularly ion exchange resins, lend themselves to tablet formulation. Furthermore, the present application teaches at page 2, lines 2-4, that tablets comprising aliphatic amine polymers of the present invention require a significant addition of other materials to assist in the tableting process. Therefore, based on the prior art cited by the Examiner, one skilled in the art could not, without additional guidance, reasonably expect to produce a tablet comprising at least 95% by weight of an aliphatic amine polymer, if one was even able to produce a tablet.

Applicants have now demonstrated that a tablet and a capsule (e.g., a Renagel capsule) are not equivalent, and that one skilled in the art would not expect that a tablet with at least 95% by weight of an aliphatic amine polymer could be produced. Thus, claims to a tablet comprising at least 95% by weight of an aliphatic amine polymer were not obvious at the time of invention. Reconsideration and withdrawal of the rejection are requested.

C. Response for Claims 19-21

It has been found that aliphatic amine polymers enhance disintegration of tablets containing pharmaceutically-active agents. No teaching in any cited reference discloses that adding an aliphatic amine polymer to a tablet would have this surprising result. Therefore, there is no motivation to combine a pharmaceutically active agent and an aliphatic amine polymer in a

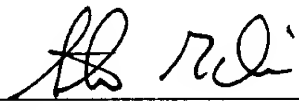
tablet. One skilled in the art would have no reason to believe that enhanced disintegration could be achieved by adding an aliphatic amine polymer to a tablet, therefore, the instant claims are nonobvious. Reconsideration and withdrawal of the rejection are requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By 

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Dated: April 12, 2002

MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

2. (Amended) A tablet [core of Claim 1] comprising a core and a coating thereof, wherein at least about 95% by weight of the core is an [the] aliphatic amine polymer [is] selected from the group consisting of unsubstistituted and N-substituted poly(allylamine), poly(diallylamine), and poly(vinylamine)[and poly(ethyleneimine)].

3. (Amended) The tablet [core] of Claim 2 wherein the N-substituents are selected from the group consisting of susbtituted and unsubstituted C_1-C_{24}-alkyl groups.

4. (Amended) The tablet [core] of Claim 3 wherein the alkyl substituents are trialkylammonioalkyl groups.

5. (Amended) The tablet [core] of Claim 2 [1] wherein the aliphatic amine polymer is cross-linked.

6. (Amended) The tablet [core] of Claim 2 [1] further comprising one or more excipients.

7. (Amended) A tablet [core] comprising a core and a coating therefor, wherein at least about 95% by weight of the core is a linear or cross-linked poly(allylamine) or a pharmaceutically acceptable salt thereof.

8. (Amended) The tablet [core] of Claim 7 wherein the poly(allylamine) is hydrated.

9. (Amended) The tablet [core] of Claim 8 wherein the poly(allylamine) comprises from about 3% to about 10% water.

10. (Amended) The tablet [core] of Claim 9 wherein the poly(allylamine) comprises from about 5% to about 8% water.

11. (Amended) The tablet [core] of Claim 10 wherein the polyallylamine is from about 1% to about 10% cross-linked.

12. (Amended) A tablet [core] comprising a core and a coating therefor, wherein at least about 95% by weight of the core is a hydrated cross-linked poly(allylamine hydrochloride).

13. (Amended) The tablet [core] of claim 2 [1] wherein the coating is [said tablet further comprises] a water-based coating.

14. (Amended) The tablet [core] of claim 7 wherein the coating is [said tablet further comprises] a water-based coating.

15. (Amended) The tablet [core] of claim 14 wherein said water-based coating comprises hydroxypropylmethylcellulose and a plasticizer.

16. (Amended) The tablet [core] of claim 15 wherein said water-based coating comprises hydroxypropyl methylcellulose low viscosity, hydroxypropylmethylcellulose high viscosity, and diacetylated monoglyceride.

17. (Amended) The tablet [core] of claim 2 wherein said polymer is polydiallylamine.

18. (Amended) The tablet [core] of claim 17 wherein said tablet further comprises a water-based coating.

19. (Amended) A compressed tablet comprising a pharmaceutically active agent and an effective disintegrating amount of polyallylamine or a salt thereof with a pharmaceutically acceptable acid.